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| 10/536,629 | 12/16/2005 | Peter Heegaard | 63528(45579) | 9252 |
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| EXAMINER | | | | |
| SCHLIENTZ, LEAH H | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/536,629

Applicant(s)

HEEGAARD ET AL.

Examiner

Leah Schlientz

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 19-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/GS/US)
Paper No(s)/Mail Date 7/13/2005

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1, claims 1-18, in the reply filed on 11/13/2009 is acknowledged. The election of species D, R, Y and Z as set forth on page 2 of the Response are also acknowledged. Claims 1-46 are pending of which claims 19-46 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1-18 are readable upon the elected invention and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a dendrimer conjugate formed between a dendrimer and a protein solubilizing substance, having the formula $D(R)_n$, "said protein solubilising substance having a structure which is not found in the dendrimer, and the conjugate--upon treatment of protein aggregates with the dendrimer conjugate--causing an increase in the solubility of protein aggregates over that obtained upon treatment of protein aggregates under the same treatment conditions with a physical mixture of the dendrimer and protein solubilising substance, the physical

mixture containing the same molar ratio of the protein solubilising substance to the dendrimer as that in the dendrimer conjugate, and the increase being evidenced by a protease assay as described herein." The claims are unclear with regard to the recitation of the "protease assay as described herein." See for Example MPEP 2173.05. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993). Reference characters corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. In the instant, the phrase "protease assay as described herein" renders the claim indefinite because the degree of increase in the solubility of protein aggregates appears to refer to that which is described in the specification and is not clearly set forth in the claims.

Claims 6, 11-13 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the

metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, the claims recites a broad recitation, such as in the case of claim 11 ranges of 0 to 20, and the claim also recites "such as e.g. 1 to 10" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomalia *et al.* (US 5,714,166) in view of Aldrich Technical Publication, 1997.

Tomalia discloses dendritic polymer conjugates which are composed of at least one dendrimer in association with at least one unit of a carried material, where the carrier material can be a biological response modifier, have been prepared. The conjugate can also have a target director present, and when it is present then the carried material may be a bioactive agent (abstract). The dendrimers for use in the conjugates of the present invention, can have terminal groups which are sufficiently reactive to undergo addition or substitution reactions. Examples of such terminal groups include amino, hydroxy, mercapto, carboxy, alkenyl, nitrile, allyl, vinyl, amido, halo, **urea**, oxiranyl, aziridinyl, etc. The dendrimers differ from conventional star or star-branched polymers in that the dendrimers have a greater concentration of terminal groups per unit of molecular volume than do conventional extended star polymers having an equivalent number of core branches and an equivalent core branch length. Thus, the density of terminal groups per unit volume in the dendrimer usually is at least 1.5 times the density of terminal groups in the conventional extended star polymer, preferably at least 5 times, more preferably at least 10 times, most preferably from 15 to 50 times. The ratio of terminal groups per core branch in the dense polymer is preferably at least 2, more preferably at least 3, most preferably from 4 to 1024. Preferably, for a given polymer molecular weight, the molecular volume of the dense

star polymer is less than 70 volume percent, more preferably from 16 to 60, most preferably from 7 to 50 volume percent of the molecular volume of the conventional extended star polymer (column 29-30).

A "dendritic polymer" is a polymer exhibiting regular dendritic branching, formed by the sequential or generational addition of branched layers to or from a core. The term "dendritic polymer" encompasses "dendrimers," which are characterized by a core, at least one interior branched layer, and a surface branched layer. A "dendron" is a species of dendrimer having branches emanating from a focal point which is or can be joined to a core, either directly or through a linking moiety to form a dendrimer. Many dendrimers comprise two or more dendrons joined to a common core. However, the term dendrimer is used broadly to encompass a single dendron. Dendritic polymer includes, but is not limited to, symmetrical and unsymmetrical branching dendrimers, cascade molecules, arborols, and the like, though the most preferred dendritic polymers are dense star polymers. The PAMAM dense star dendrimers disclosed herein are symmetric, in that the branch arms are of equal length. Dendritic polymers also encompass surface modified dendrimers. For example, the surface of a PAMAM dendrimer may be modified by the addition of an amino acid, e.g., lysine. It should be understood that reference to any particular type of dendritic polymer as a "polymer," e.g., a "dense star polymer," and "unsymmetrical dendritic polymer," a "cascade polymer" is also intended to encompass bridged dendrimers of that type, dendrimer aggregates of that type, polydisperse dendrimers of that type, and surface modified dendrimers of that type. Polyalkyleneimine (e.g.

polyethyleneimine and polypropyleneimine) dendrimers are disclosed as suitable, as are dendrimers or multiple generations (see Figures; column 42-43).

Tomalia does not specifically recite that DAB-AM-16, polypropyleneimine hecadecaamine dendrimer, is surface-modified to include a urea end group.

Aldrich Technical Publication shows that propyleneimine dendrimers are commercially available in multiple generations of diaminobutane dendrimer, including DAB(PA)16.

46,069-9 DAB(PA)4, Polypropylenimine tetraamine Dendrimer; Generation 1.0
46,072-9 DAB(PA)8, Polypropylenimine octaamine Dendrimer; Generation 2.0
46,907-6 DAB(PA)16, Polypropylenimine hexadecaamine Dendrimer; Generation 3.0
46,908-4 DAB(PA)32, Polypropylenimine dotriacontaamine Dendrimer; Generation 4.0
46,909-2 DAB(PA)64, Polypropylenimine tetrahexacontaamine Dendrimer; Generation 5.0

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide urea as an end group on a known PAMAM dendrimer; or a known polypropyleneimine dendrimer, such as DAB-AM-16 disclosed by Aldrich. One would have been motivated to do so because Tomalia teaches that dendrimers can have terminal groups which are sufficiently reactive to undergo addition or substitution reactions, including e.g. urea. One would have had a reasonable expectation of success in doing so because Tomalia teaches that a variety of dendrimers in varying generation are suitable, including both PAMAM and polyalkyleneimine dendrimers.

Regarding the limitation of claim 1, wherein "the conjugate--upon treatment of protein aggregates with the dendrimer conjugate--causing an increase in the solubility of protein aggregates over that obtained upon treatment of protein aggregates under the same treatment conditions with a physical mixture of the dendrimer and protein solubilising substance, the physical mixture containing the same molar ratio of the protein solubilising substance to the dendrimer as that in the dendrimer conjugate, and the increase being evidenced by a protease assay as described herein," it is noted that the instant claims are product claims, not method claims. The recitation of method steps such as "treatment of protein aggregate with the dendrimer conjugate" is not given patentable weight in the instant product claim.

Regarding claim 18, drawn to the EC_{50} value of 10-500 $\mu\text{g/ml}$, the claims have been examined to the extent that the structure of the dendrimer conjugate $D(R)_n$ has been addressed. Absent evidence to the contrary, a DAB dendrimer as disclosed by Tomalia having urea as a terminal group would inherently be capable of meeting the claimed functional features, such as EC_{50} value or protein solubilization, since a composition and its properties are inseparable. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's

functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS